Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

Assessment of the Negative Factors for the Clinical Outcome in Patients with SARS-CoV-2 Infection and Type 2 Diabetes Mellitus

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Purpose: Patients with diabetes mellitus (DM) are more susceptible to viral and bacterial infections, facing a more severe prognosis and higher mortality rates. The study's main aim was to evaluate the survival and mortality rates of patients with type 2 diabetes (T2DM) and SARS-CoV-2 virus infection alongside the main factors influencing the prognosis.

Patients and Methods: The present study included 186 patients with T2DM and SARS-CoV-2 virus infection admitted to the COVID-19 Department of the "Pius Brînzeu" Emergency Clinical County University Hospital between November 2020 and March 2021. Patients had investigations performed upon arrival in the emergency room and during hospitalization. We analyzed the risk of negative prognosis based on clinical data (oxygen saturation (SatO2), respiratory rate (RR), lung damage), glycemic control (HbA1c, glycemia at hospital admission), and the duration of T2DM.

Results: The mortality rate in the studied group was 36.6%. All deceased patients had previously been diagnosed with hypertension; 95.58% had a body mass index (BMI) greater than 25 kg/m^2, and 79.41% presented with cardiovascular disease (CVD). Compared to those who recovered, statistically significant differences were observed in BMI, glycemic levels at admission, glycosylated hemoglobin levels (HbA1c), SatO2, RR, and lung damage. Valid statistically significant predictors for death in T2DM patients with COVID-19 were hyperglycemia at admission > 198mg/dl, HbA1c> 8.6%, and SatO2≤ 87%.

Conclusion: SatO2, glycemia at hospital admission, and HbA1c had the highest sensitivity and specificity to predict the prognosis of T2DM patients with SARS-CoV-2 infection. Glycemic control is essential in the prognosis of patients with DM and COVID-19 infection. The prognosis was worse if other comorbidities were associated, especially hypertension and CVD.

Keywords: SARS-CoV-2 infection, type 2 diabetes mellitus, negative prognostic factors, mortality rate

Introduction

On March 11, 2020, the World Health Organization (WHO) declared the Coronavirus Infectious Disease 2019 (COVID-19) a global pandemic due to the rapid spread of this virus. Three years after the first case of COVID-19 was identified in the city of Wuhan in China, several questions related to the SARS-CoV-2 virus need to be answered.[1,2] Worldwide, nearly 700 million people have been affected, and approximately 7 million have died, causing a severe crisis in many areas.[3]

Some individuals have been more severely affected by the new SARS-CoV-2 coronavirus, namely the elderly, those with chronic diseases, respiratory diseases, cardiovascular diseases (CVD), DM, and even those with obesity presenting a higher risk of developing severe forms, even death.[4–6] T2DM represent an independent predictor for morbidity and mortality in patients with SARS-CoV-2 infection. Patients with obesity frequently present respiratory dysfunction, with changes in respiratory mechanisms, altered gas exchange, and decreased muscle strength. They risk developing more

Received: 15 November 2023
Accepted: 13 January 2024
Published: 22 January 2024

frequent severe pneumonia associated with hypoventilation and pulmonary hypertension than those without obesity. Obesity is also associated with DM, CVD, renal impairment, comorbidities that increase susceptibility to cardiovascular events, infection, and an altered immune response.[7–10]

Like all other coronaviruses, SARS-CoV-2 has four structural proteins: E (coat protein), M (membrane protein), N (nucleocapsid protein), S (spike protein), and eight accessory proteins. The spike surface glycoprotein plays an essential role by promoting the attachment of the virus to its receptor on host cells. Thus, it can determine host tropism and transmissibility.[11]

SARS-CoV-2 uses ACE-2 as a cellular entry receptor. The ACE-2 receptor is a type I transmembrane glycoprotein (mono-carboxypeptidase) composed of 805 amino acids. The first step of the viral entry process is represented by binding the N-terminal portion of the S1 viral protein to a site of the ACE-2 receptor.[12,13] After entering the host cell, the spike protein of SARS-CoV-2 is cleaved by cellular proteases, causing fusion of the viral and cellular membranes. Priming the protein spike by the transmembrane protease, serine 2 (TMPRSS2), is essential for SARS-CoV-2 infection and spreads throughout the body.[14–16]

ACE-2 receptors are present in the heart (coronary artery endothelium, myocytes, fibroblasts, epicardial adipocytes), blood vessels (endothelial and smooth vascular cells), intestinal epithelial cells, lungs (tracheal and bronchial epithelial cells, type 2 pneumocytes, macrophages), kidneys (luminal surface of tubular cells), testis and brain. The large surface area of alveolar epithelial cells could explain the increased vulnerability and severe consequences of virus invasion in the lungs.[17–23] By binding the ACE-2 receptors in the pancreas, the SARS-CoV-2 virus could change carbohydrate metabolism. Another possible explanation is the body's exaggerated response, with high antibody production that excessively acts on essential organs to maintain a normal blood glucose level.[10,24–26]

Our study aimed to evaluate the mortality and recovery rate of the negative prognostic factors in patients with T2DM and COVID-19. We analyzed the comorbidities and the cardiometabolic parameters in those who died and recovered.

Materials and Methods

We identified 1207 adult patients hospitalized in the COVID-19 Department of the "Pius Brînzeu" Emergency Clinical County University Hospital in Timisoara between November 2020 and March 2021 for a retrospective, non-randomized, non-interventional study. Patients were included in the final analysis based on the inclusion criteria: age > 18 years, previous T2DM diagnosis, confirmed SARS-COV2 infection through real-time reverse transcription–polymerase chain reaction (RT–PCR) method, pulmonary clinical signs (acute or clinically manifest respiratory failure, lung damage on the computer tomography (CT)). Patients without pulmonary clinical signs or previously known T1DM were excluded from the analysis (Figure 1). Assuming a diabetes prevalence of 10.5%, we calculated that a minimum of 145 sample size is needed to reach a confidence level of 95%. The informed consent was waived due to the retrospective study design. The study followed the ethical principles of the current Helsinki Declaration (2013 version) for medical research on human

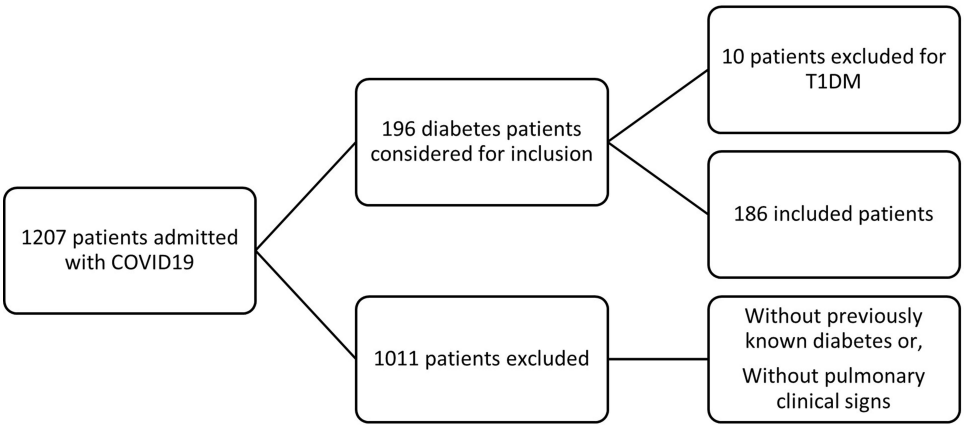

Figure 1 Diagram of the study design.

subjects and was approved by the Ethical Committee of "Pius Brînzeu" Emergency Clinical County University Hospital (416/15.11.2023), respecting the confidentiality of patients' personal data, according to General Data Protection Regulation (GDPR) Compliance.

The patients were evaluated in the hospital's emergency department before admission. The evaluation consisted of laboratory analyses, RT–PCR SARS-COV2, and pulmonary CT interpreted by artificial intelligence to establish the lung damage of COVID-19. All the clinical data of interest in this study were extracted from the clinical observation sheets of hospitalized patients: age, sex, BMI, diabetes duration, RR, oxygen saturation levels at admission (SatO2), lung damage, admission glycemia (randomly measured), HbA1c, C-reactive protein (CRP), fibrinogen, blood count, D-Dimers, associated comorbidities, and the weather patients were vaccinated for COVID-19 (data about type of vaccine or doses were not available), or required ventilatory support in intensive care units, were collected. The associated conditions sought were hypertension, CVD, heart failure, bronchial asthma, chronic obstructive pulmonary disease (COPD), cancers, and chronic kidney disease.

Statistical Analysis

Statistical analysis was performed using SPSS statistics software (Statistical Package for the Social Science version 26, for Windows; SPSS Inc., Chicago, IL, USA). The continuous variables were presented as mean and standard deviation, median with minimum, and maximum values based on their distribution. Categorical variables were presented as absolute values and percentages. For the comparison of two sets of continuous, non-normal distributed variables, the Mann–Whitney test was applied. The chi-squared or Fisher's exact test was used to compare categorical variables. To analyze the distribution of different grades of weight status among survivors or deceased groups, Chi-squared for trend was used. Statistical logistic regression analysis was used to identify death predictors. We performed receiver operating characteristic (ROC) analysis to evaluate the performance of predictive factors for evaluating the accuracy of logistic regression models that classify subjects as recovered or deceased. The area under the receiver operating characteristic (AUROC) was presented to show how much the model could distinguish between those two groups. We calculated the risk ratio of death in patients exposed to the SARS-CoV-2 vaccine prior to infection and the odds ratio for death in vaccinated and unvaccinated groups. Missing data were introduced as empty cells and ignored by the statistical analysis program. Variables with more than 5% missing data in the studied group were not considered for analysis. A p-value < 0.05 was considered statistically significant.

Results

The final analysis included 186 patients, 54.3% men (101/186) and 45.7% women (85/186), with a mean age of 68±10 years and a median diabetes duration of 8 years. 35.4% of the subjects required intensive care during hospitalization. Regarding other comorbidities, 98.3% were hypertensive, and 96.7% had a BMI over 25 kg/m^2. Also, six patients (3.2%) were diagnosed with cancers (Table 1).

The mortality rate in the study group was 36.6% (68/186), $p< 0.0001$, with a similar rate among both men and women (Table 2). Analyzing the people who died, compared to those who recovered, we observed statistically significant differences in age, BMI, glycemia at admission, HbA1c, SatO2, RR, and lung damage (Table 2). Deceased patients were older, with a higher BMI, higher glycemia at admission in the hospital, poorer glycemic control according to HbA1c, higher CRP levels, tachypneic, with more severe lung damage and acute respiratory failure, and required ventilatory support in intensive care units in a higher percentage (96.7%, $p< 0.0001$, Table 2) compared to recovered patients. Also, 43% of analyzed patients were vaccinated against SARS-CoV-2 infection. The mortality rate among vaccinated patients was 30.9% (21/68). In contrast, among the unvaccinated ones, the mortality rate was significantly higher at 69.1% ($p< 0.0001$). Overall, the survival rate was significantly higher for patients who received the COVID-19 vaccine; the relative risk of death was 0.59, $p= 0.01$, and the odds ratio was 0.44, $p= 0.01$.

Most patients have been previously diagnosed with hypertension at a similar rate regardless of gender ($p< 0.3$). However, 79.4% of the deceased subjects had CVD, compared to a lower percentage of 50.8% in the survivor group ($p< 0.001$). The distribution of weight status was similar in both groups for normal weight, overweight, or obesity grade ($p= 0.8$, chi-squared for trend). Of the patients who survived, only one patient was diagnosed with cancer; compared to the

Table 1 The Main Characteristics of the Patients

Variable	Characteristics
Number of patients	186
Women % (n)	45.7% (85/186)
Age (years)[b]	68±10
DM duration (years)[a]	8 [5; 10]
BMI (kg/m^2)[a]	30 [28; 34]
Glycemia-1 (mg/dL)[a]	178 [131; 293]
HbA1c (%)[a]	7.9 [7; 9]
RR (breaths/minute)[a]	29 [26; 34]
Lung damage (%)[a]	40 [35; 60]
SatO2 (%)[a]	89.5 [80; 92]
CRP (mg/dL)[a]	109 [76; 186]
Fibrinogen (mg/dL)[a]	420 [313.2; 576.5]
Lymphocytes (Nr/mm^3)[a]	800 [600; 990]
Thrombocytes (Nr/mm^3)[a]	274,500 [197,000; 361,000]
D-dimer (ng/mL)[a]	596 [412; 976]
ICU % (n)	35.48% (66/186)
Comorbidities	
Hypertension % (n)	98.3% (183)
CVD % (n)	61.3% (114)
Lung disease % (n)	19.3% (36)
Cancers (all types) % (n)	3.2% (6)
Obesity (BMI> 30 kg/m^2) % (n)	60.2% (112)
Diabetes Medication n (%)	
Metformin	117 (84.2%)
SGLT2 inhibitors	3 (2.2%)
DPP4 inhibitors	13 (9.4%)
GLP-1 receptor agonists	0%
Sulfonylurea	15 (10.8%)
Insulin	25 (18%)
Diet only	6 (4.3%)

Notes: [a]median (minimum, maximum), [b] mean ± SD. BMI, body mass index (kg/m^2), Glycemia-1- glycemia at admission (mg/dl), HbA1c- glycosylated hemoglobin (%), RR-respiratory rate (breaths/minute), SatO2- oxygen saturation (%), CRP-C Reactive Protein (mg/dL), ICU- ventilator support in intensive care units, CVD-cardiovascular disease.

Table 2 Comparison of Anthropometric, Clinical, and Biological Parameters in Recovered Patients, Compared to Deceased

Variables	Recovered Patients	Deceased Patients	p value
Number % (n)	63.4% (118/186)	36.6% (68/186)	<0.0001[b]
Men % (n)	63.3% (64/101)	36.6% (37/101)	0.9[b]
Women % (n)	63.5% (54/85)	36.4% (31/85)	
Age (years)	67 [59; 74]	69.5 [65; 74]	0.01[a]
DM duration (years)	7 [5; 10]	8 [6; 10.5]	0.1[a]
BMI (kg/m^2)	30 [28; 32]	33.03±4.37	< 0.0001[a]
Glycemia-1 (mg/dL)	138 [127; 186]	309 [262; 367]	< 0.0001[a]
HbA1c (%)	7.4 [5.9; 8]	9.1 [8.7; 9.6]	< 0.0001[a]
RR (breaths/min)	28 [26; 31]	34.5 [30; 37]	< 0.0001[a]
Lung damage %	40 [30; 50]	57.5 [40; 80]	< 0.0001[a]
SatO2 (%)	91 [90; 93]	75.5 [70; 81.5]	< 0.0001[a]
CRP (mg/dL)	96.5 [73; 147]	135 [83.5; 228.5]	0.003[a]
Fibrinogen (mg/dL)	390.5 [311; 536]	455 [315.75; 680]	0.2[a]
Lymphocytes (nr/mm3)	800 [640; 980]	710 [518.5; 1100]	0.5[a]
Thrombocytes (nr/mm3)	275,000 [214,000;375,000]	262,500 [185,500; 355,000]	0.1[a]
D-dimer (ng/mL)	546 [366; 820]	765.5 [486; 1834.5]	0.001[a]
ICU % (n)	3.03% (2/66)	96.9% (64/66)	<0.0001[b]
Comparison of outcomes according to vaccination rate			
SARS-CoV-2 vaccinated % (n)	50% (59/118)	30.9% (21/68)	0.01[b]
SARS-CoV-2 not vaccinated % (n)	50% (59/118)	69.1% (47/68)	0.01[b]
p-value*	1[b*]	< 0.0001[b*]	

Notes: [a]mann–Whitney test, [b]Chi-squared test; p< 0.05 statistically significant; *p value for comparison of recovery/mortality percentages between vaccinated of unvaccinated patients. BMI- body mass index (kg/m^2), Glycemia-1- glycemia at admission (mg/dl), HbA1c- glycosylated hemoglobin (%), RR-respiratory rate (breaths/minute), SatO2- oxygen saturation (%), CRP-C Reactive Protein (mg/dL), ICU- ventilator support in intensive care units.

deceased group, there was a higher cancer rate (p= 0.02), and 16.1% had known lung disease, similar to deceased subjects (p= 0.1). The frequency of comorbidities in the studied group is presented in Table 3.

To evaluate the association of death with possible predictive factors included in the analysis, measured on a continuous scale, we built univariate and multivariate logistic regression models with potential risk factors such as SatO2, lung damage, glycemia at admission, HbA1c, RR, BMI and age, respectively outcome, death. The results indicated that for every increase of 1% in SatO2, the probability of death decreases by 54% (Nagelkerke R^2= 0.88). All the other potential risk factors were directly associated with the relative risk of death, as presented in Table 4.

To see to what extent the above factors influence the risk of death, we performed a multiple logistic regression analysis, in which the dependent variable was patients who died. The independent variables were the factors mentioned in Table 4. We included the variables if p<0.05 and gradually eliminated if p> 0.1. In the regression equation, SatO2 and glycemia at admission were retained in the model as valid predictors, with Nagelkerke R^2= 0.95 (Table 5).

Table 3 The Frequency of the Patient's Comorbidities in Patients Who Recovered Compared to Those Deceased

Outcome	Recovered (n=118)		Deceased (n=68)		P value
Comorbidities	**n**	**Frequency**	**n**	**Frequency**	
Hypertension	115	98.3%	68	100%	<0.2[b]
CVD	60	50.8%	54	79.4%	<0.001[a]
Lung disease	19	16.1%	17	25%	0.1[a]
Cancers	1	0.8%	5	7.3%	0.02[b]
Normal weight	3	50%	3	50%	0.8[c]
Overweight	44	37.2%	24	35.2%	
Obesity	71	60.1%	41	60.2%	
Overweight + Obesity	115	63.8%	65	36.1%	0.6[b]

Notes: [a]Chi-squared test, [b]Fisher exact test, [c]Chi-squared test for trend.
Abbreviation: CVD, cardiovascular disease.

Table 4 Logistic Univariate Regression Analysis of Possible Risk Factors for Death in Patients with SARS-COV2 Infection and T2DM

Variable	Coefficient	Odds ratio	95% CI	Nagelkerke R^2
SatO2%	−0.7	0.46	0.3422 to 0.6189	0.88
Lung damage %	0.05	1.05	1.0344 to 1.075	0.22
Glycemia-1 (mg/dl)	0.02	1.52	1.3650 to 1.7082	0.61
HbA1c (%)	1.05	2.88	2.0482 to 4.0596	0.38
RR (breaths/min)	0.20	1.22	1.1380 to 1.3136	0.25
BMI (kg/m^2)	0.17	1.19	1.1006 to 1.2921	0.14
Age (years)	0.04	1.04	1.0092 to 1.0752	0.04
CRP (mg/dL)	0.00	1.00	1.0024 to 1.0101	0.07
D-dimer (ng/mL)	0.00	1.00	1.0002 to 1.0008	0.08
CVD	0.67	1.96	1.2608 to 3.0699	0.10

Notes: SatO2- oxygen saturation (%), Glycemia-1- glycemia at admission (mg/dl), HbA1c- glycosylated hemoglobin (%), RR-respiratory rate (breaths/minute), BMI- body mass index (kg/m^2), CRP- C reactive protein (mg/dL), CVD-cardiovascular disease.

We constructed ROC models to evaluate the possibility of predicting death based on possible factors studied, for which the outcome was death. SatO2, glycemia at hospital admission, and HbA1c had the highest sensitivity and specificity (Figures 2–4). A glycemia >198 mg/dl at admission represents a statistically significant predictive factor of death, with a sensitivity of 82.4 and specificity of 92.4, according to the ROC curve (AUROC 0.880, p< 0.001, Figure 2).

According to the ROC curve, an HbA1c > 8.6% represents a statistically significant predictive factor of death, with a sensitivity of 75.0 and specificity of 92.4 (AUROC 0.846, p< 0.001, Figure 3).

SatO2≤ 87% at admission in the hospital represents a statistically significant predictive factor of death, with a sensitivity of 95.6 and specificity of 94.1, according to the ROC curve (AUROC 0.990, p< 0.001, Figure 4).

Table 5 Multiple Logistic Regression Analysis of Possible Risk Factors for Death in Patients with SARS-COV2 Infection and T2DM

Variable	Odds Ratio	95% CI	Coefficient	Std. Error	P
SatO2%	0.38	0.2182 to 0.6727	−0.95	0.28	<0.001
Lung damage %	0.91	0.8260 to 1.0168	−0.08	0.05	0.09
Glycemia-1 mg/dl	1.84	1.2440 to 2.7462	0.03	0.01	0.002
Nagelkerke R^2= 0.95					

Notes: SatO2- oxygen saturation (%), Glycemia-1- glycemia at admission (mg/dl).

Antidiabetic medications were tested as possible predictive factors of the outcome, but the analysis could not be performed due to the small number of patients treated with different combinations between the drug classes.

Discussion

In the present research, we analyzed the demographic, clinical, biological characteristics, associated comorbidities, and antidiabetic medications of T2DM patients and pulmonary insufficiency due to the infection with SARS-CoV2 in a Romanian cohort. We identified the predictors of in-hospital death of these patients. We identified an HbA1c> 8.6%, with a random glycemia at hospital admission above 198 mg/dL and SatO2≤ 87% at admission in the hospital, representing statistically significant predictive factors of in-hospital death.

It is known that vulnerable people (elderly, those with immune depression, comorbidities like cancers, DM, hypertension, CVD, and kidney disease) have a higher risk of infections and developing severe forms of the disease.[27,28]

Hyperglycemia occurs in approximately 25–30% of patients without DM, in critical conditions, especially under stress, through many mechanisms: the release of counter-regulatory hyperglycemic hormones, changes in insulin receptors caused by the inflammation process, and reduction of insulin secretion in pancreatic β-cells.[29] It has been shown that some Coronaviridae, such as SARS-CoV-1 or MERS-CoV, destroy Langerhans cells with the activation of the enzyme dipeptidyl peptidase 4 (DPP-4), thus causing the inhibition of insulin secretion.[30–32] Hyperglycemia was also

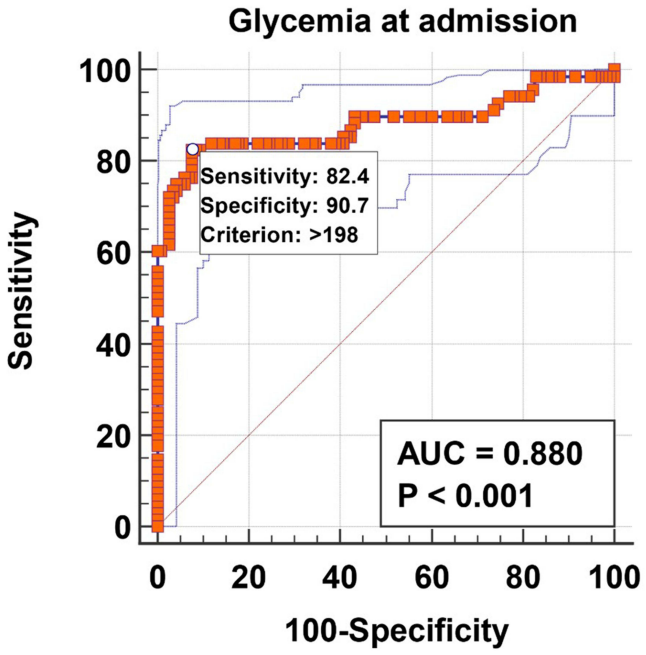

Figure 2 Graphical representation of the ROC curve of the glycemia at hospital admission for the prediction of death.

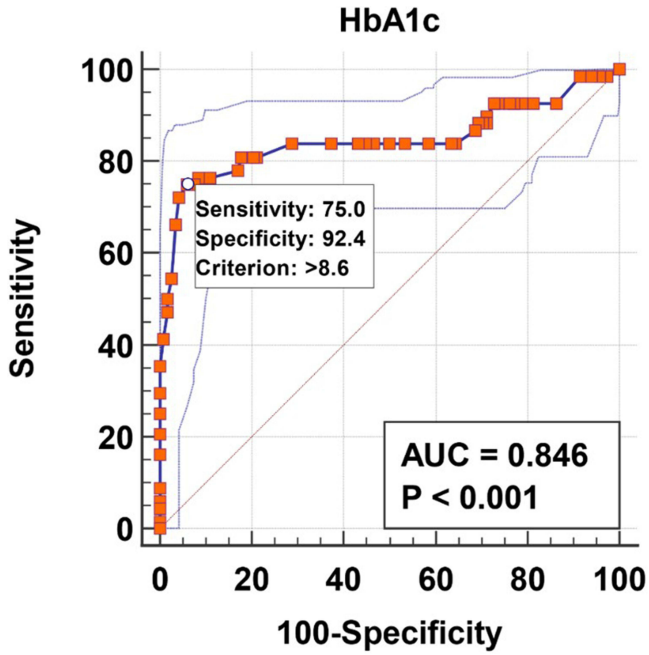

Figure 3 Graphical representation of the ROC curve of the HbA1c for the prediction of death.

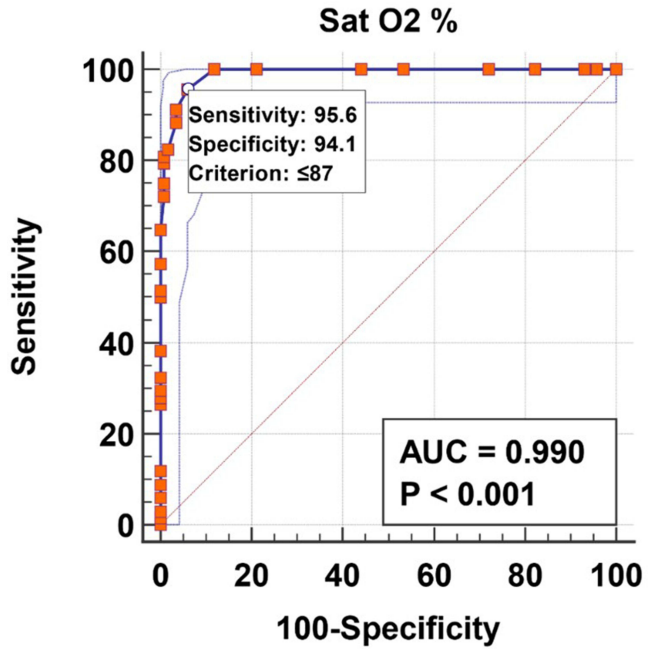

Figure 4 Graphical representation of the ROC curve of the SatO2 for the prediction of death.

detected in more than 50% of patients without previous metabolic disorders and infected with the SARS-CoV-2 virus.[33–35] Regardless of the pathophysiological mechanism involved, stress-induced hyperglycemia by an exaggerated inflammatory response is associated with endothelial dysfunction and increased oxidative stress due to the production of free radicals. These changes induce a prothrombotic state that causes cellular and tissue damage, especially in critical patients with multiple comorbidities.[36–38] In our study, patients with CVD and hypertension had a severe outcome and higher mortality rate. Patients who died had greater than 50% lung damage and SatO2 less than 80%.

Numerous studies have demonstrated that stress hyperglycemia detected at hospital admission was associated with a worse prognosis.[39] The negative prognosis can be explained by the fact that ACE-2 is the main entry receptor for SARS-CoV-2 infection, and ACE-2 glycosylation is induced by hyperglycemia.[40,41] This was also observed by Faldini et al in a retrospective analysis of 413 patients with COVID-19, in which hyperglycemia on admission was directly correlated with clinical severity and poor prognosis, especially in patients without previous DM.[42] Similar data were also demonstrated by Copelli et al.[43]

In a multivariate logistic regression analysis, Liu et al demonstrated that fasting glycemia is an independent risk factor for severe diseases.[44] Smith et al found that glycemia on hospital admission was significantly higher in patients who required oro-tracheal intubation than those who did not require ventilatory support.[45] In our group, patients who died had a statistically significant higher glycemia at hospital admission than those who recovered: 309 mg/dL compared to 138 mg/dL.

Metabolic imbalance and impaired immune system increase the susceptibility of DM patients to SARS-CoV-2 infection. A more profound knowledge of the pathophysiology of COVID-19, with the identification of metabolic mechanisms, is essential to provide specific ways to prevent and improve the consequences of SARS-CoV-2 infection.[46,47]

A significant increase in glycemic values was observed in patients with previously good glycemic control and COVID-19 infection, needing treatment with insulin therapy in higher doses. This suggests the possibility of pancreatic invasion by SARS-CoV-2. Possible mechanisms that cause damage to the pancreas are the direct cytopathic effect of SARS-CoV-2 replication, systemic response to respiratory failure, and the harmful immune response induced by SARS-CoV-2 infection.[48] Hyperglycemia activates neutrophils, contributing to the cytokine storm and sepsis in COVID-19, confirmed by increased inflammatory markers (erythrocyte sedimentation rate, CRP, ferritin, fibrinogen, D-dimers, lactate dehydrogenase).[49] A similar study shows strong positive correlations between high white blood cell counts at admission and poor outcomes. Therefore, to predict in-hospital mortality in these patients, a panel of investigations (total blood count, CRP, ferritin, systemic immune-inflammation index) is recommended.[50]

In our study, in logistic univariate regression models, we found that BMI and age are possible risk factors for in-hospital death of the study patients. Our subjects had a median BMI of 30 kg/m^2, about 35% needed intensive therapy. Similarly, in another study, COVID-19 patients with diabetes and grade I obesity were admitted to the ICU.[51] The relation between diabetes, obesity, and COVID-19 could be explained by the upregulation of ACE2 expression[52] and altered lipid synthesis and clearance, which could accelerate the inflammatory response in these patients.[53]

Age was a contributing factor to the worse outcome in the present research. Subjects who died during the hospital admission were significantly older than the survivors, with a mean difference of 2.5 years ($p< 0.01$). However, no differences across genders were observed. In an epidemiological research of 72,314 cases, 44.1% of them were elderly above 60 years old, with an increased mortality rate directly proportionally with age.[54] Researchers suggest that age, frailty, and diabetes represent the triad that aggravates the prognosis of a COVID-19 infection because of the aging immune system that makes the patient more susceptible to a severe form of infection.[54] In our study, deceased patients presented significantly higher values of CRP 135 mg/dL at the hospital admission compared to the recovered patients at 96.5 mg/dL ($p= 0.003$).

Although vaccination for preventing severe outcomes in COVID-19 was highly recommended, the vaccination status did not influence the outcome in our analysis. However, no conclusion could be drawn since we could not collect the exact data about the type of vaccine, doses, and immune response to the vaccine prior to infection with SARS-COV2.

The present study has several limitations to a lesser or greater extent. The single-center study design was retrospective observational on a relatively small number of patients. Based on the literature and policy, patients were treated according to the standard of care for their comorbidities and to the hospital protocol for COVID-19. The duration of specific symptoms before presenting at the hospital could have also been a confounding factor in the outcome. Also, data about previously administered vaccines were not available. Moreover, some patients could have been coinfected with a bacteria that influenced the prognosis.

Conclusion

SatO2, glycemia at hospital admission, and HbA1c had the highest sensitivity and specificity in predicting the prognosis of T2DM patients with SARS-CoV-2 infection. Glycemic control is essential in the prognosis of DM patients with COVID-19 infection. An optimal glycemic control may cause a lower release of inflammatory cytokines and a lower ability to bind ACE-2 to the virus, leading to improved prognosis in those affected by the SARS-CoV-2 virus. Also, SatO2 and lung damage are extremely useful factors for assessing COVID-19 prognosis. The prognosis of patients with T2DM and COVID-19 infection is worse if other comorbidities are associated, especially hypertension and CVD.

Acknowledgments

The authors gratefully acknowledge the professionals from the Diabetes, Nutrition and Metabolic Diseases Clinic, "Pius Brînzeu" Emergency Clinical County University Hospital Timisoara, Romania, for their support in data acquisition.

Disclosure

The authors report no conflicts of interest in this work.

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